SYNTHESIS AND BIOLOGICAL ACTIVITY OF 1,2,3-TRIAZOLES BASED ON ACETELENE-CONTAINING CARBAMATE DERIVATIVES

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ABSTRACT

In this article, based on propargyl ethers, copper and silver acetylenides of propargyl ethers of carbamate derivatives were synthesized, and on their basis ɣ-iodopropargyl ethers of carbamates were synthesized. By studying the influence of various factors, the optimal conditions for their synthesis have been established. The pharmacological activity and toxicity of the synthesized compounds were studied. Compounds with high anti-inflammatory activity have been identified.

Key words: carbamates, propargyl ethers, copper acetylenides, silver acetylenides, ɣ-iodopropargyl ethers, anti-inflammatory activity, toxicity.

Аннотация:в данном статье рассматривается на основе пропаргиловых эфиров были синтезированы ацетилениды меди и серебра пропаргиловых эфиров производных карбаматов, а на их основе синтезированы ɣ-йодпропаргиловые эфиры карбаматов. Изучением влияния различных факторов установлены оптимальные условия их синтеза. Исследована фармакологическая активность и токсичность синтезированных соединений. Выявлены соединения, обладающие высокой противовоспалительной активностью.

Ключевые слова:карбаматы, пропаргиловые эфиры, ацетилениды меди, ацетилениды серебра, ɣ-йодпропаргиловые эфиры, противовоспалительная активность, токсичность.

INTRODUCTION

As is known, many carbamate derivatives have a wide spectrum of biological activity. They have the ability to greatly reduce blood pressure, can lead to increased anticonvulsant properties, have psychotropic, muscle relaxant effects, have different bactericidal activity, analgesic, antitussive and local anesthetic effects [1-6]. The presence of an acetylene bond and a carbamate function allows them to be used in various other areas of the national economy. They can be used as valuable intermediates for the synthesis of herbicides, fungicides, etc. So, for example, currently monuron, diuron, simazine, atrazine, meturin, etc. are used as herbicides [7-16]. Among these compounds, carbamate derivatives are also active insecticides and herbicides. So, for example, butynylcarbamate is recommended as a herbicide, prapargoxyphenyl - N-methylcarbamates are proposed as pesticides [17-20]

In addition, the current interest in acetylene-substituted carbamate derivatives is due to a wide range of practically useful properties. Great interest in this class of compounds is caused by their high reactivity, which makes it possible to use these compounds as starting and intermediate products for the synthesis of a wide variety of classes of biologically active substances that are of great practical importance both for the needs of medical practice and for the needs of the national economy. The availability of carbamates, their versatile biological action, along with the broad synthetic capabilities of both the carbamate function and the aromatic and heterocyclic nucleus, creates a real prerequisite for their use in various directions. Many examples of the use of these compounds and their derivatives for the needs of agriculture make it possible to isolate carbamate preparations as valuable intermediates for the synthesis of herbicides, rodenticides, fungicides, natural and synthetic biologically active substances.

It should also be noted that to date, works devoted to the synthesis and study of derivatives of acetylene carbamates are insignificant. There are some works devoted to the synthesis of acetylenic carbamates based on tertiary acetylenic alcohols, dihydric alcohols of the limiting and unsaturated series. The reactivity of the obtained compounds has not been fully studied.

PURPOSE OF THE WORK

To continue our research in the field of synthesis of new carbamate derivatives - to synthesize new carbamate derivatives ɣ-bromopropargyl ethers of carbamate derivatives, with the aim of their further use as starting compounds in the synthesis of symmetric and asymmetric diacetylene ethers of carbamate derivatives.

In connection with the above, it seemed interesting to us to synthesize new acetylene-containing carbamate derivatives, in particular, to synthesize propargyl ethers, β-iodopropargyl ethers and metal containing carbamate acetylenides.

MATERIALS AND METHODS

Infra-red spectra on a UR-20 and UR-10 spectrometer (Zeiss, GDR) in the range of 3600-500 cm-1, in the form of tablets pressed with KBr.

Thin layer chromatography was used to check the purity of the obtained compounds. An AI2O3 II layer of activity degree was used as an adsorbent, and iodine vapor was used as a developer.

Results and discussion: In order to study the reactivity of terminal hydrogen in propargyl ethers of carbamate derivatives, we carried out a bromination reaction.

The replacement of acetylenic hydrogen in propargyl ethers of carbamates with bromine is carried out with the participation of equimolar amounts of propargyl carbamates and CuBr2 in an organic solvent.

We used ɣ-bromopropargyl ethers of carbamate derivatives in the synthesis of symmetric and asymmetric diacetylene ethers of carbamate derivatives.

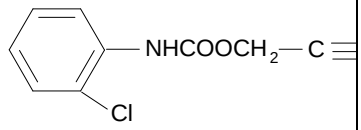
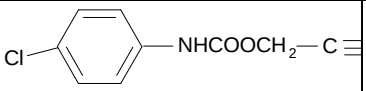
Propargyl ethers of carbamates were obtained by the interaction of propargyl alcohol with monoisocyanate in dry benzene in the presence of triethylamine according to the following scheme:

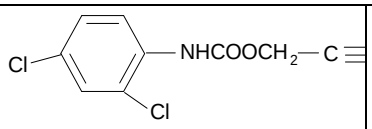
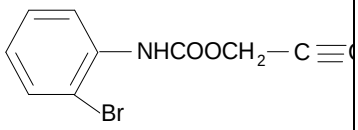
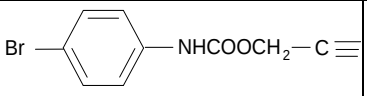
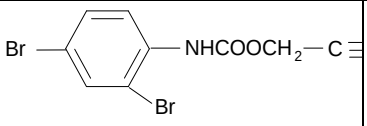
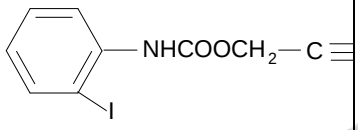
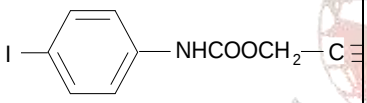
$$R - N{=}C{=}O + HO\text{-}CH_2\text{–}\ C{\equiv}CH \longrightarrow R\text{-}NH - COO\text{-}\ CH_2 - C{\equiv}CH$$

where: R= 2-CI-C_6H_4(I); 4- CI-C_6H_4(II); 2,4- CI-C_6H_3(III); 2-Br-C_6H_4(IV); 4- Br-C_6H_4(V); 2,4-Br-C_6H_3(VI); 2-I-C_6H_4(VII); 4-I-C_6H_4(VIII);

The physicochemical characteristics of the synthesized compounds are shown in the table.

Physicochemical characteristics of propargyl ethers of carbamate derivatives

№	*Formula*	*Output, %*	*Melting point, ^0C*	*Found N,%*	*Gross formula*	*Calculated N,%*
1		90.3	89-90	6.7 6.74	$C_{10}H_8ClNO_2$	6.68
2		78	90-91	6.63 6.7	$C_{10}H_8ClNO_2$	6.68

3		94.1	65-66	5.66 5.72	$C_{10}H_7Cl_2NO_2$	5.74
4		88.5	83-84	5.48 5.55	$C_{10}H_8BrNO_2$	5.51
5		90.5	73-74	5.50 5.53	$C_{10}H_8BrNO_2$	5.51
6		94.1	95-96	4.18 4.21	$C_{10}H_7Br_2NO_2$	4.20
7		92	98-99	4.6 4.7	$C_{10}H_8INO_2$	4.65
8		95.1	113-114	4.62 4.66	$C_{10}H_8INO_2$	4.65

To prove the structure of the compounds obtained, their Infrared and Proton-magnetic spectra were taken.

So in the infrared spectra of propargyl ethers there are absorption bands characteristic of CH, -C C-, -NH, NH-COO- groups. For example, the band at 3320cm-1 corresponds to stretching vibrations of the terminal acetylene bond, the absorption band at 2130cm-1 is due to stretching vibrations of the monosubstituted acetylene bond, vibrations of the NH group are characterized by an absorption band at 3340cm-1, an absorption band at 1710cm-1 due to stretching vibrations of the NH-COO-group.

EXPERIMENTAL CHEMISTRY

Infrared spectra on a UR-20 and UR-10 spectrometer (Carl Zeiss firm, GDR) in the range of 3600-500 cm-1, in the form of tablets pressed with KBr.

Thin layer chromatography was used to check the purity of the obtained compounds. An AI2O3 II layer of activity degree was used as an adsorbent, and iodine vapor was used as a developer.

Reproducibility was obtained within ± 0.02 - 0.05 values of Rf, which is apparently associated with fluctuations in the thickness of the applied layer.

In this case, when using a mixture of petroleum ether with methanol and petroleum ether and ether for propargyl ethers, quite satisfactory Rf values are achieved (from 0.77 to 0.89), while in a petroleum ether-toluene mixture they are not separated, Rf varies from 0, 03 to 0.08.

Thus, more polar solvents were used in chromatography due to the presence of a free NH-group in the compounds obtained by us, which is strongly sorbed by aluminum oxide and gives them acidic properties.

4-Chlorophenylcarbamate propargyl ether. 3.76 g of 4-chlorophenyl carbamate dissolved in anhydrous benzene and a solution of 1.12 g of propargyl alcohol in anhydrous benzene were stirred, 1-2 drops of triethylamine were added while cooling with ice water and left overnight at room temperature. Purification of the target product was carried out by thin layer chromatography on the AI2O3II degree of activity.

4-chlorophenol propargyl ether is a colorless needle crystals with so pl. 90-910C. Exit 78% of theory.

Copper acetylide of 4-chlorophenylcarbamate propargyl ether. A solution of copper monochloride taken in excess in 120ml 25%

An ammonia solution was slowly poured with stirring to a solution of 2.44 g of 4-chlorophenylcarbamate propargyl ether in 100 ml of ethanol. The resulting bright yellow precipitate was filtered off, washed, and dried.

Copper acetylide of 4-chlorophenylcarbamate propargyl ether is yellow crystals, with so decomp. 1470C. The yield is 80.4%.

Silver acetylide of 4-chlorophenylcarbamate propargyl ether.

Silver nitrate in the amount of 1.7 g dissolved in 80 ml of ethanol with vigorous stirring was poured into an alcohol solution of 2.44 g of 4-chlorophenyl carbamate propargyl ether. To the resulting flocculent precipitate was added 200 ml of distilled water. The precipitate was washed with water until the characteristic reaction of silver with halogen was absent, then washed with alcohol and sulfuric ether.

Silver acetylide of 4-chlorophenylcarbamate propargyl ether is a white crystalline substance that darkens when exposed to light. T. razl. 1230C. The yield is 78.3%.

ɣ-iodopropargyl ether of 4-chlorophenylcarbamate.

In a three-necked flask was placed 3.05 g of copper acetylide of 4-chlorophenylcarbamate propargyl ether and 400 ml of dry sulfur ether was added. With vigorous stirring, elemental iodine was added piece by piece until the color of the reaction medium stopped changing. Then the reaction mixture was stirred for another two hours at room temperature (18-200C). At the end of the time, the contents of the flask were filtered off and the filtrate was evaporated.

The obtained ɣ-iodopropargyl ether of 4-chlorophenylcarbamate is an orange crystalline substance. M.p. 90-910S. The output is 83.7% of theory.

CONCLUSIONS

1. Convenient methods have been developed for the preparation of new acetylene-containing esters of carbamate derivatives

2. Carrying out a substitution reaction based on propargyl ethers synthesized new copper and silver-containing organometallic compounds of carbamate derivatives.

3. By carrying out the iodination reaction on the basis of acetylenides, new ɣ-iodopropargyl ether of substituted carbamates were obtained.

4. Based on the study of the influence of various factors (temperature, nature of the solvent, nature of the base) on the yield of the target products, the optimal conditions for their synthesis have been established.

5. Studied the pharmacological activity of the new synthesized compounds. It was found that the synthesized new derivatives of carbamates have a wide spectrum of anti-inflammatory action. It was revealed that the compound ɣ-iodopropargyl ether 2,4-dichlorophenylcarbamate has a greater breadth of anti-inflammatory action in comparison with the well-known anti-inflammatory drug, such as amidopyrine and hydrocortisone.

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